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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/651,846	08/31/00	HLA T	UCT-0012

023413
CANTOR COLBURN, LLP
55 GRIFFIN ROAD SOUTH
BLOOMFIELD CT 06002

HM22/0410

EXAMINER	
SCHMIDT,M	
ART UNIT	PAPER NUMBER
1635	8

DATE MAILED: 04/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/651,846	Applicant(s) HLA ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-32 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2, drawn to methods of inducing angiogenesis via administration of sphingosine-1-phosphate or derivatives therof, classifiable in class 514, subclass 762.

II. Claims 3-4, drawn to methods of treatment of tumors, rheumatoid arthritis, diabetic retinopathy, Kaposi's sarcoma, hemangioma, or psoriasis, comprising administration of antagonists of signal transduction of EDG-1 or EDG-3, classifiable in class 514, subclass 2, 23 or 44, for example.

III. Claims 5-11, drawn to methods of treatment of inhibiting angiogenesis via administration of antisense to an EDG protein receptor, classifiable in class 514, subclass 44.

IV. Claims 12-17, drawn to methods for promoting cell growth and morphogenesis via administration of a bioactive substance that induces signal transduction by a G protein-coupled receptor, classifiable in class 514, subclasses 2 or 44, for example.

V. Claims 18-20, drawn to antisense oligonucleotide compositions, classifiable in class 536, subclass 24.5.

VI. Claims 21-22 and 27, drawn to methods for protecting endothelial cells from apoptotic cell death via administration of sphingosine-1-phosphate or derivatives therof, classifiable in class 514, subclass 23.

VII. Claims 23-24, drawn to methods for increasing at least one of the VE-cadherin, alpha-catenin, beta-catenin, or gamma-catenin at endothelial cell-cell junctions via administration of sphingosine-1-phosphate or derivatives therof, classifiable in class 514, subclass 23.

VIII. Claims 25-26, drawn to methods for modulating vessel maturation via administration of sphingosine-1-phosphate or derivatives therof, classifiable in class 514, subclass 23.

IX. Claims 28-30, drawn to methods for protecting endothelial cells from apoptotic cell death via administration of antisense oligoncucleotides to EDG-1, classifiable in class 514, subclass 44.

X. Claims 31 and 32, drawn to methods for inducing angiogenesis via administration of vectors expressing an EDG-R receptor, classifiable in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different

inventions have different modes of operation. Invention I is drawn to methods for inducing angiogenesis via administration of a lipid compound whereas Invention X is drawn to methods for inducing angiogenesis via administration of a vector, a plasmid or adenoviral vector, for overexpression of EDG.

3. Inventions I, IV, VII, VIII and VI are unrelated from each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects. Invention I is drawn to methods for inducing angiogenesis, Invention IV is drawn to methods for promoting cell growth and morphogenesis, Invention VII is drawn to methods for increasing one of VE-cadherin, alpha-catenin, beta-catenin or gamma-catenin, Invention VIII is drawn to methods of modulating vessel maturation, Invention VI is drawn to methods for protecting endothelial cells from apoptotic cell death. Although each of the above Inventions contemplates administration of lipid compositions, they all comtemplate a different end point function in vivo, i.e. a different physiological effect and thus require a separate set of consideratations in the art.

4. Any one of Inventions IV, VII, VIII or VI are unrelated to Invention X. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation. Inventions IV, VII, VIII and VI are drawn to methods for administering lipids for various biologic

effects whereas Invention X is drawn to administering vector compositions for expression of EDG receptors. Invention X thus operates via a different mechanism than is contemplated by the methods of the other inventions.

5. Inventions IX and III are unrelated from each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects. The methods of Inventions IX and III are both drawn to methods of delivery of antisense oligonucleotides. Invention IX is drawn to methods of protecting endothelial cells from apoptotic cell death whereas Invention III is drawn to methods of inhibiting angiogenesis. The methods thus have different end points, ie. different physiological effects which require a separate set of considerations in the art.

6. Inventions II and either IX or III are unrelated from each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects. The methods of Inventions IX and III are both drawn to methods of delivery of antisense oligonucleotides. Invention II is drawn to methods of delivery of any antagonist of signal transduction of EDG-1 and EDG-3. Invention IX is drawn to methods of protecting endothelial cells from apoptotic cell death whereas Invention III is drawn to methods of inhibiting angiogenesis. Invention II is drawn to methods of treatment of either tumors, rheumatoid arthritis, diabetic retinopathy, Kaposi's sarcoma,

hemangioma, or psoriases. The methods thus have different end points, ie. different physiological effects which require a separate set of considerations in the art.

7. Inventions I, IV, VII, VIII and VI are unrelated from either of IX or III. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation. The methods of Inventions I, IV, VII, VIII and II are drawn to methods of administering lipids whereas Inventions IX and III are drawn to methods of administering antisense oligonucleotides.

8. Invention X is unrelated from either of IX, II or III. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions. The methods of Invention X are drawn to methods of administering vectors for overexpression of EDG whereas Inventions IX, II and III are drawn to methods of administering antisense oligonucleotides and other antagonists of EDG receptors.

9. Invention V is unrelated from any of Inventions I, X, IV, VII, VIII, VI or III. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects. The compositions of Invention V are not capable of use with the methods of Inventions I, X, IV, VII,

VIII, VI or III since these methods are drawn to methods involving administration of lipid compositions which for instance would induce angiogenesis (Group I) as opposed to methods of use of the antisense which when administered would inhibit angiogenesis (such as in Group III).

10. Inventions V and either III or IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case antisense compositions of Group V can be used as probes in other assays such as Southern Blots for detection of the complementary DNA sequence.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their divergent classification and recognized divergent subject matter, and since the search required for each of Groups I, II, III, IV, V, VI, VII, VIII, IX or X is not required for the other Groups, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently

named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader* may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
April 3, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER